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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/408,578	09/29/1999	ARNE HOLM	P63882US0	4214

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	27

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/408,578	Applicant(s) HOLM ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Claims

Claims 16-42 and 46-65 have been cancelled in the present amendment of 3/21/03.

Claims 66-83 have been added and currently under examination.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly amended claims 66-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antigenic peptide sequence of Borrelia burgdorferi and iminodiacetic acid as the bridging group, does not reasonably provide enablement for any type of ligand presenting assembly containing any peptide chain or its homologs or mimics, with any achiral di or tri or tetra carboxylic acid as a bridging group and any type of chemical moiety, target or marker group that elicits an immune response under any given conditions of synthesis. The specification does not enable any person skilled in the art to which it pertains, or with which it

is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons advanced in the last Office action.

Response to Arguments

Applicants submit that the general applicability of the acids as iminodiacetic acid, amino glutaric acid, glutaric acid and tricarballylic acid is demonstrated in the Examples. Furthermore, applicants submit that the general application of the method for preparing LPA for presentation of peptide sequences has been illustrated by a wide number of sequences from different sources as illustrated in the Examples 1-12. In reply, claim 66 does not recite any specific peptides as illustrated in the Examples. Rather, the claims recite synthesis of any broad LPA. Furthermore, none of the Examples disclose T or B cell epitopes, all or part of it or mimics thereof (claim 74), or peptide sequences comprising non-naturally occurring amino acids or PNA (claim 73) or other broad components employed in the general synthesis method. The Roberts reference, newly cited by applicants, does not disclose solid phase synthesis of the Bdr protein family of Borrelia burgdorferi.

(It is suggested that applicants limit the scope of the claim to the peptide sequences and dicarboxylic acid disclosed

in the Examples, as argued, since SSPS needs sequences for the peptide to be synthesized).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Newly amended claims 66-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 66 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the providing step recited in step (a). It is not clear how said ligands are provided using the solid phase synthesis. It is further unclear as to the method of step (b) which connotes optional selection of deprotecting any one of the N-terminus of any of peptides in the ligands. This is inconsistent with the specification disclosure wherein more than one ligand is formed after step (c). See, for example, Example 1. The metes and bounds of the number, length and kinds of ligands present in a LPA, within the claimed

context, are indefinite. Also, it is not clear within the claimed context what constitutes a presenting assembly and the context of how such assembly is presented. The process step of "providing" is not a positive, manipulative process step. It is not clear how the "ring structure" is formed by simply adding the carboxylic acid. It is not clear as to the residues linked such that a ring structure is formed, especially since there is a number of ligand present in an assembly. (Note the specification recites only dimer formation). It is not evident whether such dimer is a linear or cyclic from the given structure.

B). Claim 72 and 73 are inconsistent and broadens the base claim 66. The base claim does not recite for an additional chemical entity at the N-terminus of the achiral carboxylic acid and recites an N-protected group. The metes and bounds of the chemical entity, target and marker, within the claimed context, are indefinite.

C). Claim 74 is unclear as to the metes and bounds of the B or C epitopes of the peptide sequences or mimics thereof i.e., what are included or excluded from the claims. Furthermore, it is not clear within the claimed context, "mimics" thereof i.e., in what context the peptide sequences is considered a mimic.

D). Claim 75 is unclear as to the basis by which a peptide sequence is considered to be "important" for an immune response.

E). Claims 76, 78-79 and 82-83 are indefinite as to the step or kind of the least one of the peptide sequences derived from Ospc protein of Borrelia or flagellum. The specification does not provide positive support as to the differences in the sequences of these proteins.

F). Claim 80 does not have Seq. ID. Nos. for the different recited sequences.

G). Claims 82 and 83 are duplicates of claim 66 since the same method steps are recited except for the preamble as from which the peptide is derived. The specification does not teach a peptide derived from any one of parts of Borrelia from which it is derived.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66-71 are rejected under 35 U.S.C. 102(a) as being anticipated by Lange et al(J. Pept. Sci.) or 102(b) by Gilon et al (Pept. Chem. , Proc. Jpn. Symp.) for reasons advanced in the last Office action.

Response to Arguments

Applicants submit that the present claims have been limited to a construct having a ring structure comprising the carboxylic acid and two ligands comprising the peptide sequences and intermolecular cyclization. It is argued that Lange or Gilon does not teach or suggest a construct having a ring structure comprising the carboxylic acid and two ligands comprising the peptide sequences. In response, the broadly claimed dicarboxylic acid having numerous substituents does not preclude the dicarboxylic acid of Lange. (Note further the statement in the disclosure, page 13, lines32-33 that with the "exception of glycine all amino acids have a alpha carbon atom including the amino dicarboxylic acids aspartic and glutamic acid", presupposing that only glycine is achiral.) Thus, the method of Lange would have inherently prevented racemization since the major product produced is the dimeric product.

Gilon, as admitted by applicants in the previous responses, formed cyclic peptides by cyclizing the amino groups of the mentioned amino acids in positions 6 and 9 with dicarboxylic acids, to form the lactam rings. But argue that the lactam rings are different from the products of the present invention in that the cyclization of Gilon is intramolecular as compared to intermolecular cyclization of the present invention. Applicants' argument is not commensurate in scope with the claims. The claims do not differentiate an intra from intermolecular cyclization. There is nothing in the broad claimed method steps that lead to an intermolecular cyclization of the product. In fact, it is not clear whether the dimeric product is in cyclized form.

Accordingly, the method of each of Lange and Gilon, which employs specific products and specific dicarboxylic linking group, anticipates the broad claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 66-79 and 81-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathiesen (WO97/422210) and Tomalia et al (Angew. Chem. Intl. Ed. Engl.) in view of any one of Lange for reasons advanced in the last Office action.

Response to Arguments

Applicants submit that the scope of Lange is synthesis of dimeric bradykinin(Bk) antagonists containing diamino dicarboxylic acid bridge residues. This type of compound and the scope of the problem to be solved are decisively different from the compounds and the scope of the present invention. In response, it is not clear as to the applicants' scope of the problem to be solved. Since Lange and the scope of the present invention is drawn to known solid phase synthesis of compounds. The fact is, at the time of applicants' invention, solid phase synthesis has markedly advanced that it is now automated. Given a peptide sequence, one can readily synthesize said sequence by automated synthesis, with or without a modified residue as the dicarboxylic acid. While applicants admit that even if Lange is a prior art reference, the bridging technique with half equivalent suberic acid coupled to one equivalent of lysine

attached to the synthesis resin appears slow and takes place over up to 4 days. In response, the length of synthesis does not detract from the findings that the peptide has been synthesized. One having ordinary skill in the art would expect such slow reaction. This is for this reason that automation took place. Applicants argument as to the use of excess reagent to hasten SSPS is not commensurate in scope with the claims which does not recite for any conditions of the synthesis but simply a general synthesis. Applicants further argued the synthesis of the peptide chain being longer than 4-residue, as demonstrated in the instant Examples. Matthiesen or Tomalia discloses the length of the peptide sequences.

Claim 80 is free of prior art and would be allowable with the specifics of the synthesis (fragment coupling), specifically the steps that lead to ring formation and do not cause racemization.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-32179. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1627

tdw
5/29/03